10/815,090

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	4	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	5	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	6	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	7	MAR 02	GBFULL: New full-text patent database on STN
NEWS	8	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	9	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	10	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	11	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	12	MAR 22	PATDPASPC - New patent database available
NEWS	13	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	14	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	15	APR 04	EMBASE - Database reloaded and enhanced
NEWS	16	APR 18	New CAS Information Use Policies available online
NEWS	17	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	18	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
NEWS	19	MAY 23	GBFULL enhanced with patent drawing images
NEWS	20	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
NEWS	21	MAY 26	STN User Update to be held June 6 and June 7 at the SLA 2005 Annual Conference
NEWS	22	JUN 06	STN Patent Forums to be held in June 2005
NEWS	23	JUN 06	The Analysis Edition of STN Express with Discover! (Version 8.0 for Windows) now available

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FILE 'HOME' ENTERED AT 17:40:17 ON 12 JUN 2005

=> fil reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:40:24 ON 12 JUN 2005
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STRUCTURE FILE UPDATES: 10 JUN 2005 HIGHEST RN 852098-52-3
DICTIONARY FILE UPDATES: 10 JUN 2005 HIGHEST RN 852098-52-3

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

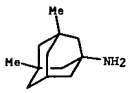
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s (memantine hydrochloride)/cn
L1 1 (MEMANTINE HYDROCHLORIDE)/CN

=> d l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 41100-52-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Adamantanamine, 3,5-dimethyl-, hydrochloride (7CI)
OTHER NAMES:
CN 1-Amino-3,5-dimethyladamantane hydrochloride
CN 3,5-Dimethyltricyclo[3.3.1.13,7]decan-1-amine hydrochloride
CN Akatinol
CN Axura
CN Ebixia
CN Ebixza
CN from Axura
CN **Memantine hydrochloride**
CN Namenda
CN NSC 102290
CN SUN Y7017
MF C12 H21 N . Cl H
CI COM
LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (19982-08-2)



● HCl

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

46 REFERENCES IN FILE CA (1907 TO DATE)
46 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     8.16       8.37

FILE 'CAPLUS' ENTERED AT 17:42:46 ON 12 JUN 2005
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FILE COVERS 1907 - 12 Jun 2005  VOL 142 ISS 25
FILE LAST UPDATED: 10 Jun 2005  (20050610/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s 41100-52-1/rn
            46 41100-52-1
             0 41100-52-1D
L2          46 41100-52-1/RN
                (41100-52-1 (NOTL) 41100-52-1D )

=> d l2 1-46 abs ibib hitstr
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L2 ANSWER 1 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB The invention is directed to formulations of pharmaceutical compds., such as the cyclohexylamines and aminoadamantanes which have antimicrobial properties. In particular, it is directed to aqueous based formulations with reduced amts. of preservatives which allow safe and convenient administration and flexible dosing and which, in the case of oral formulations, are easy to swallow. Optionally, the compns. contain components that provide the requisite stability and shelf life while reducing or avoiding incrustation of the composition around the container closure which leads to leaks and difficulty in opening the container. Solns. were prepared containing memantine-HCl or Neramexane mesylate.

ACCESSION NUMBER: 2005:423729 CAPLUS
DOCUMENT NUMBER: 142:469279
TITLE: Antimicrobial aqueous solutions comprising cyclohexylamines and aminoadamantanes
INVENTOR(S): Dedhiya, Mahendra G.; Mahashabde, Shashank; Yang, Yan; Goel, Anshu; Seiller, Erhard; Hauptmeier, Bernhard
PATENT ASSIGNEE(S): Merz Pharma G.m.b.H. & Co. K.-G.a.A., Germany
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005044228	A2	20050519	WO 2004-US37026	20041105

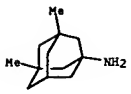
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-517981P P 20031105

IT 41100-52-1, Memantine hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimicrobial aqueous solns. comprising cyclohexylamines and aminoadamantanes)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 1 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

L2 ANSWER 2 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB A new method of preparing memantine hydrochloride, comprises the following steps: reaction of 1-bromo-3,5-dimethyladamantane and urea/formic acid with formic acid also acting as the solvent; hydrolysis with aqueous inorg. acid; alkalination, extracting and acidifying with hydrochloric acid; finally collecting target compound The method uses cheaper raw materials and conducts in homogeneous phase under mild conditions. It can reach high yield and good product purity, and be suitable for large scale production The purity of crude product is 99.0%, and reaches 99.98% after first recrystn., yield: 69.5%, bp: 332°C (DSC).

ACCESSION NUMBER: 2005:238942 CAPLUS
DOCUMENT NUMBER: 142:279886
TITLE: A method of preparing memantine hydrochloride
INVENTOR(S): Zhang, Fuli; Hu, Meng; Zhao, Lizhi; Ge, Mengya
PATENT ASSIGNEE(S): Shanghai Institute of Pharmaceutical Industry, Peop. Rep. China; Zhejiang Kangyu Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023753	A1	20050317	WO 2003-CN1094	20031219

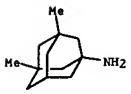
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: CN 2003-150892 A 20030910
OTHER SOURCE(S): CASREACT 142:279886

IT 41100-52-1P, Memantine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of memantine hydrochloride)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 2 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB The present invention provides a method of treating a cognitive dysfunction in a mammal. The method includes administering to the mammal an effective amount of a compound of choline esters (e.g., stearyl choline chloride). Comparison of donepezil hydrochloride (I) and stearyl choline chloride (II) in scopolamine impaired rats is reported. Animals treated with II also tended to learn the spatial location of the hidden platform faster and more efficiently than animals treated with I. Formulation of sustained-release pharmaceuticals containing active ingredients are also disclosed.

ACCESSION NUMBER: 2005:182612 CAPLUS
DOCUMENT NUMBER: 142:254637
TITLE: Choline esters useful for the treatment of cognitive dysfunctions and enhancement of memory, learning and cognition
INVENTOR(S): Patel, Hasmukh B.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019157	A1	20050303	WO 2004-US23400	20040720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005038116	A1	20050217	US 2003-642455	20030815
WO 2005018631	A1	20050303	WO 2003-US27062	20030829
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
US 2003-642455 A 20030815
WO 2003-US27062 A 20030829
US 2004-578503P P 20040608

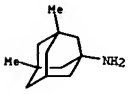
OTHER SOURCE(S): MARPAT 142:254637

IT 41100-52-1, Memantine hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(choline esters useful for treatment of cognitive dysfunctions and enhancement of memory, learning and cognition)

RN 41100-52-1 CAPLUS

L2 ANSWER 3 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB 1-Amino-3,5-dimethyladamantane hydrochloride, useful in medicinal practice for treatment of such diseases as Parkinson's disease, neurodegenerative disorders or glaucoma (no data), is prepared by addition of HNO3 to a previously prepared 1,3-dimethyladamantane emulsion in HOAc at 10-30°, followed by addition of a 30-55% aqueous urea solution at mole ratios of 1,3-dimethyladamantane to HOAc to HNO3 to urea = 1:3-4:9-12:2.5-5.0, resp., and subsequent neutralization of the reaction mass obtained with an aqueous alkali solution, extraction and isolation of product as its hydrochloride and its crystallization from H2O. This method provides a high-quality product (m.p. = 324-328°, vs. >300° by prior art) that satisfies requirements of Pharmacopoeia. In an example, treating 68 mL 1,3-dimethyladamantane in 82 mL HOAc with 190 mL fuming HNO3 at 15-20°, then after 2h adding 140 g of a 50% solution of urea at 20-25° and holding for 1 h at 25°, heating to 110 over 2 h and holding at that temperature for 2 h, then cooling and adding 400 mL of a 30% NaOH solution at 70° and subsequent extraction into PhMe and treatment with 30 mL HCl solution gave 92% 1-amino-3,5-dimethyladamantane hydrochloride.

ACCESSION NUMBER: 2005:147670 CAPLUS
DOCUMENT NUMBER: 142:240121
TITLE: Process for preparation of 1-amino-3,5-dimethyladamantane hydrochloride from urea and 1,3-dimethyladamantane
INVENTOR(S): Klimochkin, Yu. N.; Leonova, M. V.; Timofeeva, A. K.
PATENT ASSIGNEE(S): OOO "Tsiklan", Russia; AO "Olainskii Khimiko-Farmatsevticheskii Zavod"
SOURCE: Russ., No pp. given
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2246482	C2	20050220	RU 2002-135270	20021225

PRIORITY APPLN. INFO.:
RU 2002-135270 20021225

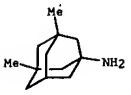
OTHER SOURCE(S): CASREACT 142:240121

IT 41100-52-1P, 1-Amino-3,5-dimethyladamantane hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of amino(dimethyl)adamantane hydrochloride from urea and dimethyladamantane in presence of nitric acid in acetic acid)

RN 41100-52-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 4 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

L2 ANSWER 5 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

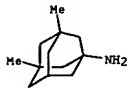
AB Compns. are provided including a neuroprotective amine related to adamantane and a polyanionic polymer which are well tolerated, non-toxic and/or result in reduced or fewer side effects. Methods are provided employing such compns., for example, topically administering such compns. to human or animal eyes, for treating human or animal eyes. Topical memantine HCl in a CMC-based formulation was tolerated up to 1.5 % w/v memantine.

ACCESSION NUMBER: 2005:122600 CAPLUS
DOCUMENT NUMBER: 142:191307
TITLE: Compositions and methods comprising memantine and polyanionic polymers for neuroprotection of eyes
INVENTOR(S): Hughes, Patrick M.; Olejnik, Orest; Schiffman, Rhett
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 752,125.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005031652	A1	20050210	US 2004-941272	20040105
PRIORITY APPLN. INFO.:			US 2004-752125	A2 20040105

IT 41100-52-1, Memantine hydrochloride
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memantine and polyanionic polymers for neuroprotection of eyes)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 6 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB Memantine HCl is prepared by chlorinating 1,3-dimethyladamantane with tert-Bu chloride in the presence of AlCl3 catalyst to obtain 1-chloro-3,5-dimethyladamantane, substituting with acetamide at 20-120° for 0.5-5 h to obtain 1-acetylamino-3,5-dimethyladamantane, alcoholizing with ethylene glycol or glycerol in the presence of NaOH, extracting with Et acetate, concentrating, salifying with HCl gas, and recrystg. in ethanol-Et acetate.

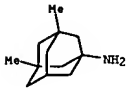
ACCESSION NUMBER: 2004:1100167 CAPLUS
DOCUMENT NUMBER: 142:316499
TITLE: Preparatio of memantine hydrochloride
INVENTOR(S): Zhou, Xingqin; Xiang, Jingde; Cao, Guoxian; Hu, Mingyang; Yang, Min; Qin, Xiaofeng
PATENT ASSIGNEE(S): Jiangsu Institute of Atomic Medicine, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1488622	A	20040414	CN 2003-132331	20030812
PRIORITY APPLN. INFO.:			CN 2003-132331	20030812

OTHER SOURCE(S): CASREACT 142:316499

IT 41100-52-1P, Memantine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of memantine hydrochloride)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 7 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB This invention relates to an oral dosage form containing between 1 mg and 100 mg of memantine, wherein said dosage form does not contain 10 mg of memantine or 20 mg of memantine, and wherein said dosage form is not prepared by the patient or a person administering the drug to the patient who divides the dosage form containing a larger dose of memantine. Other aspects of this invention relate to pharmaceutical products comprising the oral dosage forms and methods of administering memantine for treating glaucoma. For example, memantine-HCl 4.00% and Avicel PH101 4.00% were milled, blended with Lactose Fast Flo 69.61%, Avicel PH302 16.84%, Croscarmellose sodium 5.00%, Cab-O-Sil 0.25%, and Mg stearate 0.30%, and compressed into tablets. Tablets (5 mg memantine) were then coated first with a purple coating comprising Opadry Purple 03B10434 2.00 parts and water 14.67 parts, followed by a glaze coating comprising Opadry Clear YS-1-19025-A 0.25 parts and water 4.75 parts. Tablets comprising 5 mg of memantine were administered daily to a patient suffering from glaucoma for 2 wk, followed by a tablet comprising 10 mg of memantine daily for 2 wk. At the beginning of the 4th wk of the treatment, a tablet comprising 15 mg of memantine was administered daily for as long as the drug is needed.

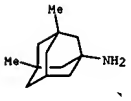
ACCESSION NUMBER: 2004:1082036 CAPLUS
DOCUMENT NUMBER: 142:62712
TITLE: Memantine oral dosage forms
INVENTOR(S): Firestone, Bruce A.; Vander, Zanden J. Jacob; Terwilliger, Rodney J.; Cheetham, Janet K.; Kurjan, Richard; Kuan, Teresa H.; Chang, Chin-ming; Espiritu, J. Abraham M.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004254251	A1	20041216	US 2004-869169	20040615
WO 2004112768	A1	20041229	WO 2004-US18506	20040610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2003-478979P	P 20030616

IT 41100-52-1, Memantine hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of memantine tablets for glaucoma treatment)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 7 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

L2 ANSWER 8 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB The invention relates to a simple and improved osmotic device for the controlled release of an active agent from the core into the use environment. According to the invention, the active agent is first released through a preformed passage and, subsequently, through a second passage which is formed in situ. Optionally, the size of one or both of the passages increases during the use of the osmotic device. Moreover, the preformed passage and/or the second passage increases the release speed of the active agent and enables the release of larger particles containing the active agent and/or the release of active agents which are essentially insol. in the use environment. Owing to the in situ formation of the second opening, the device can release a greater percentage of active agent than that which would be released without said second opening.

ACCESSION NUMBER: 2004:1036887 CAPLUS
DOCUMENT NUMBER: 142:11520
TITLE: Breakable, controlled-release tablets comprising a preformed passage
INVENTOR(S): Facur, Joaquina; Vergez, Juan A.
PATENT ASSIGNEE(S): Osmotica Costa Rica, Sociedad Anonima, Costa Rica
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103349	A2	20041202	WO 2004-CR5	20040521
WO 2004103349	A3	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

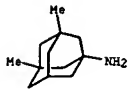
US 2005008702	A1	20050113	US 2004-851866	20040521

PRIORITY APPLN. INFO.: US 2003-472819P P 20030522

IT 41100-52-1, Memantine hydrochloride
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(breakable, controlled-release tablets comprising a preformed passage)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 8 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

L2 ANSWER 9 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

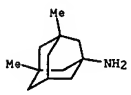
AB A review. Memantine (Axura, Merz Pharmaceuticals GmbH; Ebixa, H. Lundbeck A/S, Namenda, Forest Labs., Inc.) is an uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist with low to moderate affinity for the (+)MK-801 binding site. It is characterized as a voltage-sensitive open-channel NMDA receptor blocker that antagonizes NMDA receptor-mediated inward currents in vitro with an IC50 of 1-3 μM. In animal models, memantine displays both neuroprotective (antiexcitotoxic) and cognition-enhancing properties at therapeutically relevant concns. The strong voltage dependency and rapid blocking/unblocking kinetics of memantine are thought to be the basis for its excellent clin. tolerability. Recently completed clin. studies demonstrate pos. effects of memantine in Alzheimer's disease both as a monotherapy and in patients receiving continuous donepezil treatment. Memantine treatment also has demonstrated significant improvement of cognitive performance in patients suffering from vascular dementia. Furthermore, the safety and tolerability of memantine in clin. trials has been excellent, with the incidence of premature withdrawals due to adverse events no greater than placebo and overall low frequencies of total adverse events. In 2002, memantine was approved by the European Medicines Agency (EMEA) for the treatment of moderately severe to severe Alzheimer's disease. More recently, memantine was approved in the US for the treatment of moderate to severe Alzheimer's disease (Oct. 2003). Here, we review the most recent pharmacol. and clin. data in dementia patients that has emerged from the systematic evaluation of memantine.

ACCESSION NUMBER: 2004:909501 CAPLUS
DOCUMENT NUMBER: 142:189916
TITLE: Memantine hydrochloride: pharmacological and clinical profile
AUTHOR(S): Moebius, Hans J.; Stoeffler, Albrecht; Graham, Stephen M.
CORPORATE SOURCE: Merz Pharmaceuticals, Frankfurt, Germany
SOURCE: Drugs of Today (2004), 40(8), 685-695
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

IT 41100-52-1, Axura
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Namenda, Ebixa; memantine hydrochloride pharmacol. and clin. profile)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 9 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



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REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS

L2 ANSWER 10 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

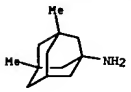
AB Objective: The aim of the present study was to predict the drug interaction potential of memantine by elucidation of its inhibitory effects on cytochrome P 450 enzymes using pooled human liver microsomes (HLM) and recombinant P450s. Methods: The inhibitory potency of memantine on CYP1A2, CYP2A6, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4 activities was examined with specific probe drugs in HLM and recombinant P450s. The in vivo drug interactions of memantine were predicted in vitro using the [I]/([I] + KI) values. Results: In HLM, memantine inhibited CYP2B6 and CYP2D6 activities, with KI (IC50) values of 76.7 (279.7) and 94.9 (368.7) μM, resp. Both inhibitions were competitive. In addition, cDNA-expressed P450s were used to confirm these results. Memantine strongly inhibited recombinant CYP2B6 activity with IC50 (KI) value of 1.12 (0.51) μM and activity of recombinant CYP2D6 with IC50 (KI) value of 242.4 (84.4) μM. With concns. up to 1,000 μM, memantine showed no appreciable effect on CYP1A2, CYP2E1, CYP2C9, or CYP3A4 activities and a slight decrease of CYP2A6 and CYP2C19 activities. Based on [I]/([I] + KI) values calculated using peak total plasma concentration (or enzyme-available concentration in the liver) of memantine and the KI obtained in HLM, 1.3 (13.5), and 1.0 (11.2), inhibition of the clearance of CYP2B6 and CYP2D6 substrates could be expected, resp. Nevertheless, when considering KI values obtained from cDNA-expressed CYP2B6, as generally recommended, even 66.2 (95.9) decrease in metabolism of coadministered CYP2B6 substrates could be anticipated. Conclusion: Memantine exerts selective inhibition of CYP2B6 activity at clin. relevant concns., suggesting the potential for clin. significant drug interactions. Inhibition of other CYPs during memantine therapy is unlikely. Moreover, memantine represents a new, potent, selective inhibitor of recombinant CYP2B6, which may prove useful for screening purposes during early phases of in vitro drug metabolism studies with new chemical entities.

ACCESSION NUMBER: 2004:870590 CAPLUS
DOCUMENT NUMBER: 142:190169
TITLE: Inhibitory effects of memantine on human cytochrome P450 activities: prediction of in vivo drug interactions
AUTHOR(S): Micuda, Stanislav; Mundlova, Lucie; Anzenbacherova, Eva; Anzenbacher, Pavel; Chladek, Jaroslav; Fuksa, Leos; Martinkova, Jirina
CORPORATE SOURCE: Department of Pharmacology, Medical Faculty of Charles University, Hradec Kralove, 500 38, Czech Rep.
SOURCE: European Journal of Clinical Pharmacology (2004), 60(8), 583-589
CODEN: EJCPAS; ISSN: 0031-6970
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(noncompetitive NMDA antagonist memantine exerted inhibitory effect on CYP2B6 with weak or no influence on metabolic activities of CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4 using human liver microsomes and recombinant P 450)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 10 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

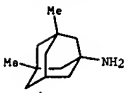
AB The inotropic Glu receptors N-methyl-D-aspartate (NMDA) and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors are present peripherally in the primary sensory afferent neurons innervating the viscera. Multiple studies have reported roles of Glu receptors in gastric functions. However, no study has previously shown the direct influence of inotropic Glu receptor antagonist on vagal sensory neurons. The objective of this study was to investigate the effects of NMDA and AMPA receptor antagonists on mechanotransduction properties of vagal afferent fibers innervating the rat stomach. Action potentials were recorded from the hyponodal vagus nerve innervating the antrum of the Long-Evans rats. For antral distension (AD), a small latex balloon was inserted into the stomach and positioned in the antrum. The antral contractions were recorded with solid-state probe inserted into the water-filled balloon. Antral units were identified to isovolumic (0.2-1 mL) or isobaric AD (5-60 mm Hg). NMDA and AMPA receptor antagonists were injected in a cumulative fashion (1-100 μmol/kg, i.v.). After the conclusion of experiment, the abdomen was opened and receptive field was mapped by probing the serosa of the stomach. Thirty-two fibers were identified to AD. The receptive fields of 26 fibers were located in the posterior part of the antrum. All fibers exhibited spontaneous firing (mean: 7.00 impulses/s). Twenty fibers exhibited a rhythmic firing that was in phase with antral contractions, whereas 12 fibers exhibited non-rhythmic spontaneous firing unrelated to spontaneous antral contraction. Both groups of fibers exhibited a linear increase in responses to graded isovolumic or isobaric distensions. NMDA (memantine HCl and dizocilpine (MK-801)) and AMPA/kainate (6-cyano-7-nitroquinoxaline 2,3-dione; CNQX) receptor antagonists dose-dependently attenuated the mechanotransduction properties of these fibers to AD. However, competitive NMDA antagonist DL-2-amino-5 phosphopentanoic acid (AP-5) had no effect. The study documents that Glu receptor antagonists can attenuate responses of gastric vagal sensory afferent fibers innervating the distal stomach, offering insight to potential pharmacol. agents in the treatment of gastric disorders.

ACCESSION NUMBER: 2004:322482 CAPLUS
DOCUMENT NUMBER: 140:417661
TITLE: Response properties of antral mechanosensitive afferent fibers and effects of ionotropic glutamate receptor antagonists
AUTHOR(S): Sengupta, J. N.; Petersen, J.; Peles, S.; Shaker, R.
CORPORATE SOURCE: MaccFund Research Center, Division of Gastroenterology and Hepatology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
SOURCE: Neuroscience (Oxford, United Kingdom) (2004), 125(3), 711-723
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response properties of antral mechanosensitive afferent fibers and effects of inotropic Glu receptor antagonists)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

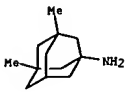
L2 ANSWER 11 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB Memantine HCl was synthesized from 1,3-dimethyladamantane by bromination, acetamidation with acetonitrile in H_2SO_4, and hydrolysis with an overall yield of 67.8%.
ACCESSION NUMBER: 2003:1011883 CAPLUS
DOCUMENT NUMBER: 141:53977
TITLE: Synthesis of memantine hydrochloride
AUTHOR(S): Zou, Yong; Xiong, Xiaoyun; Mei, Qibing
CORPORATE SOURCE: Guangzhou Institute of Chemistry, Chinese Academy of Sciences, Guangzhou, 510650, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2003), 34(5), 213-214
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 141:53977
IT 41100-52-1P, Memantine hydrochloride
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of memantine hydrochloride)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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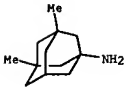
L2 ANSWER 13 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB The objectives of this study were to characterize sepia, synthetic, and bovine melanin and to determine their binding characteristics to the drug memantine. Phys. methods were used to characterize sepia, synthetic, and bovine melanin. Their binding properties toward memantine were determined in deionized water and phosphate-buffered saline (PBS) at 37°. Melanin-memantine binding was measured indirectly by determining the unbound fraction of memantine. Curve fitting according to the Langmuir binding isotherm for one binding site was used for the determination of binding capacity (BLmax) and dissociation constant (KD). Synthetic and sepia melanin had comparable Gaussian particle size distributions, whereas bovine melanin showed a heterogeneous distribution profile. The suspension medium had a small effect on the particle size distribution of synthetic and bovine melanin. There were characteristic differences in the IR spectra of the melanins. The rank order for BLmax in deionized water was sepia > bovine > synthetic melanin. However, when the melanins were suspended in PBS, the BLmax values were lower, and the rank order was bovine > sepia > synthetic. Whereas the KD values for sepia and synthetic melanin remained largely the same in deionized water and PBS, the KD value for bovine melanin in PBS was more than twice than in deionized water. This study showed that the phys. characteristics of the melanins investigated differ markedly. The binding of memantine to melanin is thought to be determined by the different chemistries of the melanins, particle size, and buffer electrolytes.
ACCESSION NUMBER: 2003:814624 CAPLUS
DOCUMENT NUMBER: 140:292422
TITLE: Binding of Memantine to Melanin: Influence of Type of Melanin and Characteristics
AUTHOR(S): Koeberle, Martin J.; Hughes, Patrick M.; Skellern, Graham G.; Wilson, Clive G.
CORPORATE SOURCE: Strathclyde Institute for Biomedical Sciences, Department of Pharmaceutical Sciences, University of Strathclyde, Glasgow, UK
SOURCE: Pharmaceutical Research (2003), 20(10), 1702-1709
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 41100-52-1, Memantine hydrochloride
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binding of memantine to melanin)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 13 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



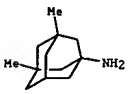
● HCl

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB This invention pertains to a method for producing memantine•HCl by reacting 1-bromo-3,5-dimethyladamantane with urea in a polyol solvent (such as HOCH2CH2OH), followed by treatment with NaOH, and acidification with hydrochloric acid (70-78%). The title compound can be used as an N-methyl-D-aspartic acid (NMDA) receptor antagonist for curing dementia (no data). This method features safe and simple operation and low cost.
ACCESSION NUMBER: 2003:626610 CAPLUS
DOCUMENT NUMBER: 139:133274
TITLE: Process for preparation of memantine hydrochloride
INVENTOR(S): Zou, Yong; Zhu, Jie; Xiong, Xiaoyun
PATENT ASSIGNEE(S): Guangzhou Inst. of Chemistry, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1400205	A	20030305	CN 2002-134628	20020830

PRIORITY APPLN. INFO.: CN 2002-134628 20020830
OTHER SOURCE(S): CASREACT 139:133274
IT 41100-52-1P, Memantine hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of memantine hydrochloride)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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L2 ANSWER 15 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB Pharmaceutical conjugates are disclosed which have a therapeutic component and an efficacy-enhancing component that enhances the pharmacokinetic disposition of the therapeutic component. In one embodiment, the therapeutic component is joined to an efficacy-enhancing component by a linker. In one embodiment, the therapeutic component and the efficacy-enhancing component disassoc. under physiol. conditions, preferably near the site where the therapeutic component may exert a therapeutic effect. The efficacy-enhancing component is an adamantane derivative, e.g. a memantine.

ACCESSION NUMBER: 2003:473262 CAPLUS
DOCUMENT NUMBER: 139:30756
TITLE: Adamantane derivative-containing pharmaceutical conjugates with enhanced pharmacokinetic characteristics
INVENTOR(S): Hughes, Patrick M.; Olejnik, Orest
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

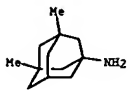
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003114460	A1	20030619	US 2001-16850	20011214
CA 2471589	AA	20030626	CA 2002-2471589	20021213
WO 2003051400	A1	20030626	WO 2002-US40153	20021213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1455837	A1	20040915	EP 2002-795884	20021213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005516017	T2	20050602	JP 2003-552332	20021213
PRIORITY APPLN. INFO.:			US 2001-16850 A	20011214
			WO 2002-US40153 W	20021213

OTHER SOURCE(S): MARPAT 139:30756

IT 41100-52-1, Memantine hydrochloride
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adamantane derivative-containing pharmaceutical conjugates with enhanced pharmacokinetic characteristics)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 15 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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L2 ANSWER 16 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

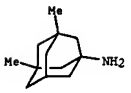
AB Alzheimer's disease (AD) is a devastating illness that causes enormous emotional stress to affected families and is associated with substantial medical and nonmedical costs. To determine the effects of 28 wk of memantine treatment for patients with AD on resource utilization and costs, a multicenter, prospective, double-blind, randomized, placebo-controlled clin. trial was performed in the US. The Wilcoxon-Mann-Whitney test was used to examine the resource utilization variables and logistic regression models were used for multivariate resource utilization analyses. Anal. of covariance (ANCOVA) models (log and non-log) were computed to examine costs from a societal perspective. All costs were calculated in 1999 US dollars. Outpatients with moderate to severe AD were studied. Overall, 252 patients received randomized treatment, and 166 patients (placebo n = 76, memantine n = 90) formed the treated-per-protocol (TPP) subset for the health economic analyses, on which the main cost anal. was based. The main outcome measure was the Resource Utilization in Dementia (RUD) scale, measuring patient and caregiver resource utilization, and various sources for cost calcns. Controlling for baseline differences between the groups, significantly less caregiver time was needed for patients receiving memantine than for those receiving placebo (difference 51.5 h per mo; 95% CI -95.27, -7.17; p = 0.02). Anal. of residential status also favored memantine: time to institutionalization (p = 0.052) and institutionalization at week 28 (p = 0.04 with the chi-square test). Total costs from a societal perspective were lower in the memantine group (difference $US1089.74/mo [non-overlapping 95% CI for treatment difference -1954.90, -224.58]; p = 0.01). The main differences between the groups were total caregiver costs ($US-823.77/mo; p = 0.03) and direct nonmedical costs ($US-430.84/mo; p = 0.07) favoring memantine treatment. Patient direct medical costs were higher in the memantine group (p < 0.01) mainly due to the cost of memantine. Resource utilization and total health costs were lower in the memantine group than the placebo group. The results suggest that memantine treatment of patients with moderate to severe AD is cost saving from a societal perspective.

ACCESSION NUMBER: 2003:341302 CAPLUS
DOCUMENT NUMBER: 139:79012
TITLE: Resource utilisation and cost analysis of memantine in patients with moderate to severe Alzheimer's disease
AUTHOR(S): Wimo, Anders; Winblad, Bengt; Stoeffler, Albrecht; Wirth, Yvonne; Moebius, Hans-Joerg
CORPORATE SOURCE: Division of Geriatric Epidemiology (Sector of Health Economy), Neurotec, Karolinska Institute, Huddinge, Swed.
SOURCE: PharmacoEconomics (2003), 21(5), 327-340
CODEN: PARMEK; ISSN: 1170-7690
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(resource utilization and cost anal. of memantine in patients with moderate to severe alzheimer s disease)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 16 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

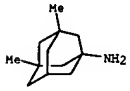
L2 ANSWER 17 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB The process comprises acetylaminating 1-bromo-3,5-dimethyladamantane with acetonitrile in the presence of H_2SO_4, pouring into ice/water, precipitating at 0-5° for 10-14 h to obtain 1-acetylamino-3,5-dimethyladamanthane; treating with polyol (such as 1,2-ethanediol) in the presence of NaOH, extracting with chloroform, concentrating, acidifying with HCl, and recrystg. in chloroform.

ACCESSION NUMBER: 2003:238375 CAPLUS
DOCUMENT NUMBER: 138:221260
TITLE: Synthesis of memantine hydrochloride
INVENTOR(S): Zou, Yong; Xiong, Xiaoyun; Wei, Wen
PATENT ASSIGNEE(S): Guangzhou Inst. of Chemistry, Academia Sinica, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1335299	A	20020213	CN 2001-127788	20010829
CN 1125033	B	20031022		

PRIORITY APPLN. INFO.: CN 2001-127788 20010829
OTHER SOURCE(S): CASREACT 138:221260
IT 41100-52-1P, Memantine hydrochloride
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of memantine hydrochloride)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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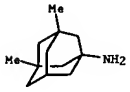
L2 ANSWER 18 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB 5-Amino-1,3-dimethyltricyclo[3.3.1.13,7]decane hydrochloride is prepared in high yield and selectivity by the amination of 5-chloro-1,3-dimethyltricyclo[3.3.1.13,7]decane with formamide, followed by extraction of the intermediate with toluene and salification with aqueous hydrochloric acid.

ACCESSION NUMBER: 2002:644318 CAPLUS
DOCUMENT NUMBER: 137:140294
TITLE: Amination process for preparing the hydrochloride of 5-amino-1,3-dimethyltricyclo[3.3.1.13,7]decane from 5-chloro-1,3-dimethyltricyclo[3.3.1.13,7]decane and formamide
INVENTOR(S): Kysilka, Vladimir; Zizkova, Vera; Bystra, Dagmar; Palasova, Lenka
PATENT ASSIGNEE(S): Lachema, A. S., Czech Rep.
SOURCE: Czech Rep., 4 pp.
CODEN: CZXXED
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CZ 288445	B6	20010613	CZ 1996-1813	19960620

PRIORITY APPLN. INFO.: CZ 1996-1813 19960620
OTHER SOURCE(S): CASREACT 137:140294
IT 41100-52-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(amination process for preparing the hydrochloride of 5-amino-1,3-dimethyltricyclo[3.3.1.13,7]decane from 5-chloro-1,3-dimethyltricyclo[3.3.1.13,7]decane and formamide)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

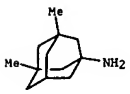


● HCl

L2 ANSWER 19 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB A review, discussing the action mechanism and pharmacol. of memantine hydrochloride, a new possible agent for Alzheimer's disease.

ACCESSION NUMBER: 2002:604203 CAPLUS
DOCUMENT NUMBER: 138:147016
TITLE: Memantine hydrochloride, a new possible agent for Alzheimer's disease
AUTHOR(S): Kihara, Tetsuroh
CORPORATE SOURCE: Pharmaceutical Div., Project Planning Development, Suntory Limited, Japan
SOURCE: BIO Clinica (2002), 17(9), 802-805
CODEN: BCILCY; ISSN: 0919-8237
PUBLISHER: Hokuryukan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
IT 41100-52-1, Memantine hydrochloride
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memantine hydrochloride, a new possible agent for Alzheimer's disease)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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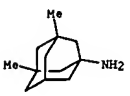
L2 ANSWER 20 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB A review. Memantine hydrochloride, an NMDA antagonist, was launched in Germany by Merz in 1989 for the treatment of dementia, an indication for which development was continuing in other markets. It is also under development by Merz, Lundbeck, Neurobiol. Technologies Inc (NTI), Forest Labs. and Suntory for the potential treatment of Alzheimer's disease (AD), AIDS-related dementia and pain in patients with neuropathy, and by Allergan for the potential treatment of ocular disease. By July 2001, a regulatory filing for neuropathic pain was expected in 2003. In Feb. 2002, the CPMP recommended to the EU commission to approve memantine for the treatment of moderately-severe to severe Alzheimer's disease. At this time, marketing authorization was expected late in the first half of 2002, and Lundbeck planned to launch memantine under the brand name Ebixa during the second half of 2002. Merz and Lundbeck, filed memantine for AD in the EU in Sept. 2000 and an NDA was submitted in Nov. of that year. The compound was in phase II trials in the US for the treatment of AIDS-related dementia and pain by August 1996 and phase III trials for glaucoma and neuroprotection by 1999. Analysts at Merrill Lynch predicted in Oct. 2001 that Allergan would make regulatory filings in the US for memantine in glaucoma and ocular hypertension in 2005, and that Forest Labs. would file for memantine in the US as a supplement to Alzheimer's disease data in early 2002, and for the treatment of neuropathic pain in 2003. Sales of $25 million in 2004, rising to $75 million in 2005, were predicted by Merrill Lynch for this product (429181).

ACCESSION NUMBER: 2002:580307 CAPLUS
DOCUMENT NUMBER: 137:149666
TITLE: Memantine(Merz)
AUTHOR(S): Kilpatrick, Gavin J.; Tilbrook, Gary S.
CORPORATE SOURCE: CeNeS Ltd, Cambridge, CB4 9ZR, UK
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(5), 798-806
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
IT 41100-52-1, SUN Y7017
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memantine for Alzheimer disease, AIDS dementia complex, neuropathy and ocular disease)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS

L2 ANSWER 20 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 21 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB The invention relates to the use of substances for the manufacturing of a pharmaceutical composition or medicament for the treatment of disturbances or illnesses which are linked to malfunction of an ionotropic acetylcholine receptor and/or a calcium-activated potassium channel functionally associated with said acetylcholine receptor, wherein said substance is at least one adamantane derivative

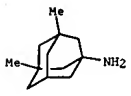
ACCESSION NUMBER: 2002:240554 CAPLUS
DOCUMENT NUMBER: 136:257271
TITLE: Treatment of diseases such as leukemia and deafness with adamantane derivatives
INVENTOR(S): Ruppersberg, J. Peter; Fakler, Bernd
PATENT ASSIGNEE(S): Tinnitus Forschungs-Und Entwicklungs G.m.b.H., Germany
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024187	A2	20020328	WO 2001-EP10927	20010921
WO 2002024187	A3	20030522		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1190711	A1	20020327	EP 2000-120660	20000921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1201234	A2	20020502	EP 2000-121508	20000929
EP 1201234	A3	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
CA 2422535	AA	20020328	CA 2001-2422535	20010921
AU 2001089903	A5	20020402	AU 2001-89903	20010921
EP 1333822	A2	20030813	EP 2001-969751	20010921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004048892	A1	20040311	US 2003-380845	20030730

PRIORITY APPLN. INFO.:
EP 2000-120660 A 20000921
EP 2000-121508 A 20000929
WO 2001-EP10927 W 20010921

OTHER SOURCE(S): MARPAT 136:257271
IT 41100-52-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of diseases such as leukemia and deafness with adamantane derivs.)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA

L2 ANSWER 21 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
INDEX NAME)



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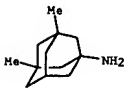
L2 ANSWER 22 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB The stability consts. for the inclusion complexes of β-cyclodextrin (β-CD) with various adamantane derivs. (ADA), namely the amantadinium (AM), rimantadinium (RIM),and memantinium (MEM) cations have been determined by UV-Vis spectrophotometry. All expts. have been performed at a pH of 1.7 and 25 °C on aqueous solns. adjusted to an ionic strength of 0.05 M (Na, H+)ClO4. The competitive binding method has been used whereby methyl orange (MO) is first encapsulated by β-CD and is then substituted by ADA. It has been shown that the derivs. studied form host-guest type complexes. The calculated stability consts., reported as log K1, were estimated to be 3.9 ± 0.1, 5.1 ± 0.2 and 3.3 ± 0.1, for AM, RIM and MEM, resp. The factors that govern the strength of binding ADA with β-CD have been discussed and an attempt was made to rationalize the variation in the established stability consts. for the ADA-β-CD complexes. General exptl. conditions required for the determination of the stability consts. of ADA with β-CD with the use of MO as an auxiliary agent were evaluated. The optimized exptl. conditions are recommended. It has been concluded that MO, even though commonly used in this type of study, does not meet the optimal and recommended conditions.

ACCESSION NUMBER: 2001:736068 CAPLUS
DOCUMENT NUMBER: 135:294641
TITLE: Stability constants of the inclusion complexes of β-cyclodextrin with various adamantane derivatives. A UV-Vis study
AUTHOR(S): Vashi, Preeti R.; Cukrowski, Ignacy; Havel, Josef
CORPORATE SOURCE: School of Chemistry, Univ. of the Witwatersrand, Johannesburg, 2050, S. Afr.
SOURCE: South African Journal of Chemistry [online computer file] (2001), 54, 1-18
CODEN: SAJCDG; ISSN: 0379-4350
URL: http://ejour.sabinet.co.za/images/ejour/chem/chem_v54_a5.pdf?sessionid=01-62329-1648007521
PUBLISHER: South African Chemical Institute
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
IT 41100-52-1, Memantine hydrochloride
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(adamantyl ammonium encapsulation with β-cyclodextrin after methyl orange displacement)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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L2 ANSWER 22 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

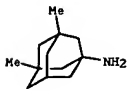
L2 ANSWER 23 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB A combined antidotal treatment with Memantine-HCl (MEM, 18 mg/kg, s.c.) and atropine sulfate (ATS, 16 mg/kg, s.c.) provided complete protection against acute carbofuran toxicity (1.5 mg/kg, s.c.) in rats by multiple mechanisms. Carbofuran, in addition to inhibiting serine-containing esterases, also perturbed the activities of mitochondrial/cytoplasmic biomarker enzymes (creatine kinase, CK; and lactic dehydrogenase, LDH) in diaphragm muscle. The observed changes in the activity of biomarker enzymes were reflected in serum as a result of their leakage from the diaphragm due to a depletion of high-energy phosphates, such as ATP (27%) and phosphocreatine (PCr, 33%) and their metabolites (ADP, 36%; AMP, 35%; and Cr, 38%). Combined treatment with MEM and ATS provided protection and reversal of the induced changes in biomarkers by preventing the depletion of the high-energy phosphates and thus maintaining normal cell membrane characteristics, including permeability and integrity. These results, along with those reported previously, indicate that MEM antagonizes carbofuran toxicity by multiple mechanisms.

ACCESSION NUMBER: 2000:194628 CAPLUS
DOCUMENT NUMBER: 133:54712
TITLE: Role of high-energy phosphates and their metabolites in protection of carbofuran-induced biochemical changes in diaphragm muscle by Memantine
AUTHOR(S): Gupta, Ramesh C.; Goad, John T.
CORPORATE SOURCE: Toxicology Department, Breathitt Veterinary Center, Murray State University, Hopkinsville, KY, 42241-2000, USA
SOURCE: Archives of Toxicology (2000), 74(1), 13-20
CODEN: ARTODN; ISSN: 0340-5761
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(role of high-energy phosphates and their metabolites in protection of carbofuran-induced biochem. changes in diaphragm muscle by Memantine)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB Pharmaceutical compds. having NMDA antagonist activity are used for treating certain conditions in the gastrointestinal tract, such as functional gastrointestinal disorders, and in particular irritable bowel syndrome (IBS). Also provided are pharmaceutical compns. for the treatment of IBS and a product comprising such compds. and a pharmaceutically acceptable carrier.

ACCESSION NUMBER: 1999:708596 CAPLUS
DOCUMENT NUMBER: 131:317787
TITLE: Use of NMDA antagonists for treatment of gastrointestinal disorders including irritable bowel syndrome
INVENTOR(S): Asghar, Aziz; Cabero, Jose Luis; Dray, Andrew; King, Anne
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955323	A1	19991104	WO 1999-SE702	19990428
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2329328	AA	19991104	CA 1999-2329328	19990428
AU 9943024	A1	19991116	AU 1999-43024	19990428
AU 760783	B2	20030522		
BR 9909971	A	20001226	BR 1999-9971	19990428
EP 1073431	A1	20010207	EP 1999-947024	19990428
EP 1073431	B1	20040707		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002512956	T2	20020508	JP 2000-545522	19990428
NZ 507436	A	20030926	NZ 1999-507436	19990428
AT 270545	E	20040715	AT 1999-947024	19990428
ES 2221753	T3	20050101	ES 1999-947024	19990428
TW 570793	B	20040111	TW 1999-88113888	19990813
NO 2000005386	A	20001026	NO 2000-5386	20001026
HK 1033876	A1	20050304	HK 2001-104450	20010627

PRIORITY APPLN. INFO.: SE 1998-1494 A 19980428
SE 1998-3954 A 19981118
WO 1999-SE702 W 19990428

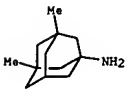
OTHER SOURCE(S): MARPAT 131:317787

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NMDA antagonists for treatment of gastrointestinal disorders including irritable bowel syndrome)

RN 41100-52-1 CAPLUS

L2 ANSWER 24 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

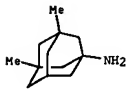
L2 ANSWER 25 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB The effects of site-specific NMDA receptor antagonists on i.v. cocaine self-administration were examined in rats trained to self-administer cocaine (0.25 mg/infusion) on a fixed ratio (FR) 5 schedule with a 20-s time-out (TO) after each reinforcer. The non-competitive NMDA receptor antagonists, dizocilpine (MK-801, (+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine hydrogen maleate) (0.05-0.2 mg/kg i.p.) and memantine (1,3-dimethyl-5-amino-adamantane hydrochloride) (2.5-20 mg/kg i.p.), dose-dependently decreased cocaine self-administration, while the competitive NMDA receptor antagonist, CGP 39551 (DL-(E)-2-amino-4-methyl-5-phosphono-3-pentanoic acid carboxyethylester) (2.5-15 mg/kg i.p.), and the NMDA/glycine receptor antagonist, L-701,324 (7-chloro-4-hydroxy-3(3-phenoxy)-phenyl-2(H)quinolone) (1.25-10 mg/kg p.o.), were without effect. Under a progressive ratio (PR) schedule, dizocilpine (0.15 mg/kg i.p.) increased the number of cocaine infusions in a manner similar to increasing the unit dose of cocaine, suggestive of potentiation of cocaine reward. Conversely, memantine (10 mg/kg i.p.) produced rate-decreasing effects on the PR schedule. These results demonstrate that NMDA receptor antagonists acting at different modulatory sites of the NMDA receptor do not share dizocilpine's cocaine reward enhancing effects although they are all known to be effective blockers of NMDA receptor activity.

ACCESSION NUMBER: 1999:546768 CAPLUS
DOCUMENT NUMBER: 131:266935
TITLE: Site-specific NMDA receptor antagonists produce differential effects on cocaine self-administration in rats
AUTHOR(S): Hyytia, Petri; Backstrom, Pia; Liljequist, Sture
CORPORATE SOURCE: Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, FIN-00101, Finland
SOURCE: European Journal of Pharmacology (1999), 378(1), 9-16
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(differential effects of NMDA receptor antagonists on cocaine self-administration in rats)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS

L2 ANSWER 25 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 26 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB 5-Aminotricyclo[3.3.1.13,7]decanes substituted with either Me or hydrogen in the 1 and/or 3 positions (e.g., 5-aminoadamantane) are prepared in high yield and selectivity by the solvolysis of the corresponding 1,3-substituted 5-(acetamino)adamantanes [e.g., 5-(acetamino)adamantane] with 0.5-1.5 parts alkali (e.g., KOH) in anhydrous MeOH, EtOH, or 2-PrOH for 10-30 h at 110-140°; acid addition salts may be prepared by the reaction of the free amine with (in)organic acids in toluene.

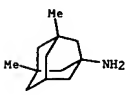
ACCESSION NUMBER: 1999:337632 CAPLUS
DOCUMENT NUMBER: 130:337866
TITLE: Solvolytic process for preparing 1,3-substituted 5-aminotricyclo[3.3.1.13,7]decanes from the corresponding acetamides in the presence of alkali
INVENTOR(S): Kysilka, Vladimir; Bystra, Dagmar; Macoun, Petr; Smekal, Oldrich; Jelinek, Jiri
PATENT ASSIGNEE(S): Lachema A. S., Czech Rep.
SOURCE: Czech Rep., 5 pp.
CODEN: CZXXED
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CZ 282398	B6	19970716	CZ 1994-863	19940413
PRIORITY APPLN. INFO.:			CZ 1994-863	19940413

OTHER SOURCE(S): CASREACT 130:337866

IT 41100-52-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solvolytic process for preparing 1,3-substituted 5-aminotricyclo[3.3.1.13,7]decanes from the corresponding acetamides in the presence of alkalis)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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L2 ANSWER 27 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB The migraine-treating effectiveness of an antimigraine drug is significantly enhanced by administering a selective 5-HT1 agonist together with dextromethorphan or dextrorphan.

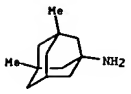
ACCESSION NUMBER: 1999:231198 CAPLUS
DOCUMENT NUMBER: 130:232532
TITLE: Method for treating migraine using antimigraine drug with 5-HT1 agonist and dextromethorphan or dextrorphan
INVENTOR(S): Caruso, Frank S.
PATENT ASSIGNEE(S): Algos Pharmaceutical Corporation, USA
SOURCE: U.S., 6 pp., Cont.-in-part of U.S. Ser. No. 727,923, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5891885	A	19990406	US 1996-736370	19961024
US 5939425	A	19990817	US 1997-858269	19970519
CA 2267893	AA	19980416	CA 1997-2267893	19971006
WO 9815275	A2	19980416	WO 1997-US17828	19971006
WO 9815275	A3	19980806		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748061	A1	19980505	AU 1997-48061	19971006
EP 932416	A2	19990804	EP 1997-910772	19971006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000508341	T2	20000704	JP 1998-517619	19971006
US 6043244	A	20000328	US 1999-226297	19990107
PRIORITY APPLN. INFO.:			US 1996-727923	B2 19961009
			US 1996-736370	A3 19961024
			WO 1997-US17828	W 19971006

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimigraine drug with 5-HT1 agonist and dextromethorphan or dextrorphan for migraine treatment)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 27 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

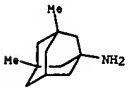
L2 ANSWER 28 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB A novel paired transcranial magnetic stimulation (TMS) paradigm with a suprathreshold first and a subthreshold second stimulus was used in healthy volunteers to investigate the acute effects of a single oral dose of various CNS-active drugs on short-interval motor evoked potential (MEP) facilitation. MEPs were recorded from the relaxed abductor digiti muscle. Three peaks of MEP facilitation were consistently observed at interstimulus intervals of 1.1-1.5 ms, 2.3-2.7 ms, and 3.9-4.5 ms. The size of these MEP peaks was transiently suppressed by drugs which enhance pgamma-aminobutyric acid (GABA) function in the neocortex (lorazepam, vigabatrin, phenobarbital, ethanol), while the GABA-B receptor agonist baclofen, anti-glutamate drugs (gabapentin, memantine), and sodium channel blockers (carbamazepine, lamotrigine) had no effect. The interstimulus intervals effective for the production of the MEP peaks remained unaffected by all drugs. The MEP peaks are thought to be due to a facilitatory interaction of I-(indirect) waves in the motor cortex. Therefore, the present results indicate that the production of I-waves is primarily controlled by GABA related neuronal circuits. The potential relevance of this non-invasive paired TMS protocol for the investigation of I-waves in patients with neurol. disease will be discussed.

ACCESSION NUMBER: 1998:616272 CAPLUS
DOCUMENT NUMBER: 130:423
TITLE: Pharmacological control of facilitatory I-wave interaction in the human motor cortex. A paired transcranial magnetic stimulation study
AUTHOR(S): Ziemann, Ulf; Tergau, Frithjof; Wischer, Stephan; Hildebrandt, Jorg; Paulus, Walter
CORPORATE SOURCE: Department of Clinical Neurophysiology, University of Gottingen, Gottingen, D-37075, Germany
SOURCE: Electroencephalography and Clinical Neurophysiology (1998), 109(4), 321-330
CODEN: ECNEAZ; ISSN: 0168-5597
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. control of facilitatory I-wave interaction in the human motor cortex)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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L2 ANSWER 28 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 29 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

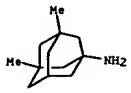
AB The effects of the GABAA receptor antagonists, pentylenetetrazol, bicuculline, and picrotoxin, the glycine antagonist, strychnine, and the NMDA receptor antagonist, memantine, on ethanol-induced behavioral sleep and body temperature were investigated. Pentylenetetrazol, bicuculline, and picrotoxin given prior and following ethanol reduced the behavioral sleep and potentiated the hypothermia caused by ethanol. However, convulsions appeared when bicuculline, but not pentylenetetrazol and picrotoxin, were given following ethanol. After the reversal of unconsciousness in rats without convulsions the animals remained awake throughout the expts. without motor incoordination, hyperexcitability, and sedation, but they were in hypothermia within 12 h. The glycine antagonist, strychnine, given prior or after ethanol had virtually no effect on ethanol-induced behavioral sleep and hypothermia. Ethanol given prior or following strychnine failed to antagonize strychnine-induced convulsions. The NMDA receptor antagonist, memantine, given following ethanol potentiated the behavioral sleep and had virtually no effect on hypothermia induced by ethanol. It is suggested that the ethanol-induced behavioral sleep may be attributed to its ability to enhance the GABAergic mechanisms and to inhibit NMDA-mediated excitatory responses. However, the ethanol-induced hypothermia may be ascribed solely to the facilitation of GABAergic transmission. Further, it is postulated that a bidirectional inhibitory system subserves the regulation of behavioral sleep and convulsions. However, one-way inhibitory system underlies the ethanol-induced hypothermia.

ACCESSION NUMBER: 1997:243380 CAPLUS
DOCUMENT NUMBER: 126:272263
TITLE: Opposite effects of GABAA and NMDA receptor antagonists on ethanol-induced behavioral sleep in rats
AUTHOR(S): Beleslin, D. B.; Djokanovid, Nada; Jovanovid-Midid, Danica; Samardaeid, Ranka
CORPORATE SOURCE: Department of Pharmacology, Medical Faculty, Belgrade, 11000, Yugoslavia
SOURCE: Alcohol (New York) (1997), 14(2), 167-173
CODEN: ALCOEX; ISSN: 0741-8329
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of GABAA and NMDA receptor antagonists on ethanol-induced behavioral sleep and hypothermia in rats)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 29 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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L2 ANSWER 30 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
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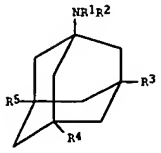


I

AB Adamantane derivs. I (R1, R2 = H, C1-6 alkyl, or R1NR2 = 5- or 6-membered ring; R3, R4 = H, C1-6 alkyl, C5-6 cycloalkyl, Ph; R5 = H, C1-6 alkyl) and their salts are useful for treatment of tinnitus, Meniere's disease, and other inner ear disorders. Thus, patients with cochlear tinnitus were treated with memantine-HCl (10 mg/day by infusion for 5 days, then 20 mg/day by infusion for 5 days, then 20 mg/day orally). Marked improvement was observed in .apprx.66% of the patients; in some cases the improvement persisted even after discontinuation of treatment.

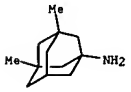
ACCESSION NUMBER: 1997:148911 CAPLUS
DOCUMENT NUMBER: 126:166505
TITLE: Adamantane derivatives for treatment of inner ear disorders
INVENTOR(S): Zenner, Hans Peter
PATENT ASSIGNEE(S): Zenner, Hans Peter, Germany
SOURCE: Ger. Offen., 2 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19528388	A1	19970206	DE 1995-19528388	19950802
CA 2228393	AA	19970213	CA 1996-2228393	19960731
WO 9704762	A1	19970213	WO 1996-EP3360	19960731
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9667882	A1	19970226	AU 1996-67882	19960731
AU 719018	B2	20000504		
EP 759295	A1	19970226	EP 1996-112325	19960731
EP 759295	B1	19980304		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 163545	E	19980315	AT 1996-112325	19960731
EP 834310	A1	19980408	EP 1997-122113	19960731

L2 ANSWER 30 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
ES 2116801	T3	19980716	ES 1996-112325	19960731
CN 1194581	A	19980930	CN 1996-196650	19960731
BR 9609950	A	19990629	BR 1996-9950	19960731
JP 2000515486	T2	20001121	JP 1997-507250	19960731
JP 3568039	B2	20040922		
IL 123142	A1	20011031	IL 1996-123142	19960731
US 6066652	A	20000523	US 1998-11085	19980612
PRIORITY APPLN. INFO.:			DE 1995-19528388 A	19950802
			EP 1996-112325 A3	19960731
			WO 1996-EP3360 W	19960731

OTHER SOURCE(S): MARPAT 126:166505
IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adamantane derivs. for treatment of inner ear disorders)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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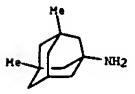
L2 ANSWER 31 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
AB N-terminal Fmoc-protected peptide combinations that form gels in water and diverse organic solvents. These types of peptides form gels in aqueous solns.
and are biol. compatible and may be useful for drug delivery, antigen delivery and may be useful as food additives to retard spoilage and act as fillers. A gel containing 10 mg/mL Fmoc-Leu-Asp was prepared and 5-methyl-1-adamantanamine-3-carboxylic acid (I) was incorporated into the gel at concentration of 33mM. When the gel containing I in phosphate buffered saline
was injected into rabbits, without adjuvant, antibodies were raised against this drug to produce antisera with titers as high or higher than those of animals immunized with I-bovine serum albumin conjugates in equal vols. of complete Freund's adjuvant.

ACCESSION NUMBER: 1995:863630 CAPLUS
DOCUMENT NUMBER: 123:266122
TITLE: Gel-forming polypeptide derivatives for drug delivery
INVENTOR(S): Vegners, Rolands; Janmey, Paul A.
PATENT ASSIGNEE(S): Brigham and Women's Hospital, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9521622	A1	19950817	WO 1995-US1890	19950209
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9519195	A1	19950829	AU 1995-19195	19950209
JP 10511340	T2	19981104	JP 1995-521421	19950209
US 5955434	A	19990921	US 1996-693215	19960809
PRIORITY APPLN. INFO.:			LV 1970-700000 A	19940209
			LV 1994-940007 A	19940209
			WO 1995-US1890 W	19950209

OTHER SOURCE(S): MARPAT 123:266122
IT 41100-52-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gel-forming polypeptide derivs. for drug delivery)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 31 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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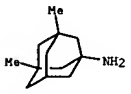
L2 ANSWER 32 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB The activation of glutamate receptors by endogenous glutamate has been implicated in the processes that underlie cell loss associated with ischemia and trauma and in the development of some neurodegenerative diseases. The antagonism of NMDA-sensitive glutamate receptors may therefore have therapeutic applications. The present study compared the side effects and neuroprotective potency of 1-aminoadamantane hydrochloride (amantadine), 1-amino-3,5-dimethyladamantane hydrochloride (memantine), and (+)-5-methyl-10,11-dihydro-5H-dibenzocyclohepten-5,10-imine maleate ((+)-MK-801) against NMDA injected directly into the nucleus basalis magnocellularis of rats. Each drug significantly attenuated the loss of nucleus basalis magnocellularis cholinergic cells. The ED50s were resp. 0.077, 2.81 and 43.5 mg/kg for (+)-MK-801, memantine and amantadine, giving a relative potency ratio of 1:36:565. The ratio of the ED50 for the side effects observed, including ataxia, myorelaxation and stereotypy, and the ED50 for neuroprotective ability, was highest for memantine and the lowest for (+)-MK-801. The results suggest that a potential neuroprotective action of NMDA receptor antagonists, memantine and amantadine in particular, can be seen at low doses lacking side effects.

ACCESSION NUMBER: 1995:847129 CAPLUS
DOCUMENT NUMBER: 123:275847
TITLE: MK-801, memantine and amantadine show neuroprotective activity in the nucleus basalis magnocellularis
AUTHOR(S): Wenk, Gary L.; Danysz, Wojciech; Mobley, Sherri L.
CORPORATE SOURCE: Arizona Research Laboratories Division of Neural Systems, Memory and Aging, 384 Life Sciences North, University of Arizona, Tucson, AZ, USA
SOURCE: European Journal of Pharmacology, Environmental Toxicology and Pharmacology Section (1995), 293(3), 267-70
CODEN: EPEPEG; ISSN: 0926-6917
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NMDA receptor antagonists MK-801 and memantine and amantadine show neuroprotective activity in nucleus basalis magnocellularis injury induced by NMDA)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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L2 ANSWER 32 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

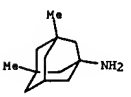
L2 ANSWER 33 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB CA1 pyramidal cell response (population spike) in the hippocampal slice preparation was monitored after elec. stimulation of the Schaffer collaterals
at CA2 in the presence of different concns. of memantine (1-amino-3,5-dimethyladamantane, Akatinol Memantine, CAS 41100-52-1) currently being prescribed for the treatment of e.g. dementia. Memantine increased the amplitude of the population spike by 100% compared to the predrug level with an EC50 of approx. 8 μmol/l. Long-term potentiation induced by a brief theta stimulus was likewise increased by a factor of 2. The concentration dependent action of D-serine, an
agonist acting at the strychnine insensitive glycine-site of the NMDA (N-methyl-d-aspartic acid) receptor was enhanced in the presence of 1 μmol/l of memantine. These effects of memantine were antagonized completely by very low concns. of the selective non-NMDA receptor antagonist NBQX (2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo (F) quinoxyline) as well as by less selective antagonist such as DNQX (6,7-dinitroquinoxaline-2,3-dione) and CNQX (6-cyano-7-nitroquinoxaline-2,3-dione). In contrast, dizocilpine tested under identical conditions and in concordance with the literature decreased long-term potentiation. Thus, memantine clearly has different effects on glutamatergic synaptic transmission compared to dizocilpine. The ability of memantine to enhance synaptic transmission in the hippocampus is in concordance with the reported pos. influence on cognition deficits in humans.

ACCESSION NUMBER: 1995:411501 CAPLUS
DOCUMENT NUMBER: 122:178277
TITLE: Effects of memantine on synaptic transmission in the hippocampus in vitro
AUTHOR(S): Dimpfel, W.
CORPORATE SOURCE: Pro Sci. Private Res. Inst. GmbH, Linden, Germany
SOURCE: Arzneimittel-Forschung (1995), 45(1), 1-5
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Cantor
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memantine effect on synaptic transmission in the hippocampus)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 33 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

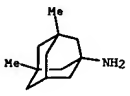
L2 ANSWER 34 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB The competitive N-methyl-D-aspartate (NMDA) receptor antagonists, DL-(E)-2-amino-4-methyl-5-phosphono-3-pentanoic acid (CGP 37849) and D(-)-2-amino-5-phosphonovaleric acid (APV), and the non-competitive NMDA antagonists, memantine and amantadine, which are used in the treatment of Parkinson's disease, were tested for their effects on intrastriatally evoked excitatory postsynaptic potentials (EPSPs) in rat neostriatal slices. Fast, non-NMDA receptor mediated synaptic excitation was not affected by any of the NMDA receptor antagonists. The NMDA component of the EPSPs was more prominent following reduction of the non-NMDA component of the EPSP by the non-NMDA receptor antagonist 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX, 5-10 μM). Memantine (30 μM) and amantadine (100 μM) had similar effects in reducing the NMDA component, but were not as effective as CGP 37849 (1-5 μM) or APV (10 μM). The data are compatible with a possible locus of action of memantine and amantadine in the neostriatum.

ACCESSION NUMBER: 1995:276696 CAPLUS
DOCUMENT NUMBER: 122:46388
TITLE: Suppression by memantine and amantadine of synaptic excitation intrastriatally evoked in rat neostriatal slices
AUTHOR(S): Rohrbacher, Jutta; Bijak, Maria; Misgeld, Ulrich
CORPORATE SOURCE: I. Physiologisches Inst., Universitaet Heidelberg, Heidelberg, D-69120, Germany
SOURCE: Neuroscience Letters (1994), 182(1), 95-8
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 41100-52-1, Memantine hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppression by NMDA receptor antagonists memantine and amantadine of synaptic excitation intrastriatally evoked in rat neostriatal slices in relation to Parkinson's disease treatment)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 35 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

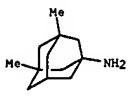
AB Nonischemic NMDA receptor-mediated neuronal damage in a mammal is reduced by administering amantadine and related compds. to the mammal. Also disclosed is a screen for antagonists of NMDA receptor-mediated neurotoxicity which have an enhanced prospect for being clin. tolerated and selective against such neurotoxicity. The amantadine derivative, memantine, prevented retinal ganglion cell death from the endogenous glutamate-related toxin in a dose-dependent manner.

ACCESSION NUMBER: 1994:261373 CAPLUS
DOCUMENT NUMBER: 120:261373
TITLE: Method of preventing NMDA receptor-mediated neuronal damage using amantadine and related compounds
INVENTOR(S): Lipton, Stuart A.
PATENT ASSIGNEE(S): The Children's Medical Center Corp., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9405275	A1	19940317	WO 1993-US8344	19930903
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5334618	A	19940802	US 1992-939824	19920903
AU 9348476	A1	19940329	AU 1993-48476	19930903
EP 660707	A1	19950705	EP 1993-921355	19930903
EP 660707	B1	20010627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08501297	T2	19960213	JP 1993-507482	19930903
AT 202474	E	20010715	AT 1993-921355	19930903
GR 3036657	T3	20011231	GR 2001-401515	20010918
PRIORITY APPLN. INFO.:			US 1992-939824 A	19920903
			US 1991-680201 B2	19910404
			WO 1993-US8344 W	19930903

IT 41100-52-1, Memantine hydrochloride
RL: BIOL (Biological study)
(retinal ganglion cell death from glutamate-related toxin prevention by)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L2 ANSWER 35 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L2 ANSWER 36 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB A dosage form with matrix-controlled 2-stage release of the active ingredient has a matrix comprising a mixture of water-soluble and water-insol. casein salts. The matrix is produced by mixing the water-soluble and water-insol. casein salts or by adding salts of di- or multivalent cations to water-soluble casein. Thus, tablets were prepared containing memantine-HCl 20.0, Na caseinate 46.8, Ca caseinate 31.2, Aerosil 200 1.0, and Mg stearate 1.0 weight%.

ACCESSION NUMBER: 1994:144211 CAPLUS
DOCUMENT NUMBER: 120:144211
TITLE: Process for producing solid pharmaceutical dosage forms with an extended two-stage release
INVENTOR(S): Nuernberg, Eberhard; Seiller, Ehrhard; Ritsert, Stefan
PATENT ASSIGNEE(S): Merz & Co. G.m.b.H. und Co., Germany
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

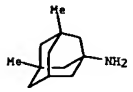
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 582186	A1	19940209	EP 1993-112018	19930728
EP 582186	B1	19990224		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 4225730	A1	19940210	DE 1992-4225730	19920804
DE 4225730	C2	20030430		
US 5382601	A	19950117	US 1993-96952	19930723
AT 176866	E	19990315	AT 1993-112018	19930728
ES 2128369	T3	19990516	ES 1993-112018	19930728
ZA 9305614	A	19950203	ZA 1993-5614	19930803
IN 176667	A	19960817	IN 1993-MA538	19930803
IL 106580	A1	19980208	IL 1993-106580	19930803
WO 9403158	A1	19940217	WO 1993-EP2074	19930804
W: AU, BR, CA, CZ, FI, HU, JP, KR, NO, PL, RU, SK, UA				
CN 1086708	A	19940518	CN 1993-116211	19930804
LT 3201	B	19950327	LT 1993-839	19930804
LV 10182	B	19950420	LV 1993-1013	19930804
JP 07509479	T2	19951019	JP 1994-505015	19930804
JP 3560244	B2	20040902		
AU 669731	B2	19960620	AU 1993-47069	19930804
AU 9347069	A1	19940303		

PRIORITY APPLN. INFO.: DE 1992-4225730 A 19920804
WO 1993-EP2074 W 19930804

IT **41100-52-1**, Memantine hydrochloride
RL: BIOL (Biological study)
(controlled-release pharmaceuticals containing, casein water-insol. and water-soluble salts in)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 36 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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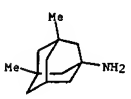
L2 ANSWER 37 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB A recently developed solid-phase binding assay was used to investigate the specificity of ligand binding to a mouse monoclonal anti-dinitrophenyl IgE (I). All DNP-amino acids, that were tested inhibited the binding of the radio-labeled I to DNP covalently attached to polystyrene microplates; however, the concentration for 50% inhibition varied within four orders of magnitude, DNP-L-serine being the most and DNP-L-proline the least potent inhibitor. In addition to DNP analogs, a large number of drugs and other compds. were tested for their ability to compete with DNP for the binding site of I. At the concentration used for screening, 59% of compds. had no significant inhibition; 19% inhibited the binding of I more than 50%. Several families of compds. (tetracyclines, polymyxins, phenothiazines, salicylates, and quinones) that were effective competitors were found. Within these families, changes in the functional groups attached to the family stem had major effects on the affinity of ligand binding. The occurrence frequencies of interactions of ligands with I is in good agreement with the semi-empirical model for multispecific antibody-ligand interactions.

ACCESSION NUMBER: 1992:400277 CAPLUS
DOCUMENT NUMBER: 117:277
TITLE: Mechanism of allergic cross-reactions. I. Multispecific binding of ligands to a mouse monoclonal anti-DNP IgE antibody
AUTHOR(S): Varga, Janos M.; Kalchschmid, Gertrud; Klein, Georg F.; Fritsch, Peter
CORPORATE SOURCE: Dep. Dermatol., Univ. Innsbruck, Innsbruck, 6020, Austria
SOURCE: Molecular Immunology (1991), 28(6), 641-54
CODEN: MOIMD5; ISSN: 0161-5890
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **41100-52-1**, Memantine hydrochloride
RL: BIOL (Biological study)
(binding of, to anti-dinitrophenol monoclonal antibody, allergic cross-reaction mechanism in relation to)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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L2 ANSWER 38 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

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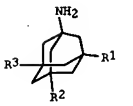


I

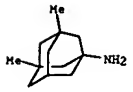
AB A series of bridgehead substituted amantadines I (R1-3 = H, Me; R1-2 = Me, Et, R3 = H; R1 = Me, Et, Pr, R2-3 = H) were prepared and tested for potential antiparkinson activity as dopamine agonists (DA). E.g., 1,3-adamantanediacetic acid was converted to its di-Me ester, which was reduced with LiAlH4 to give 83.5% 1,3-adamantanediethanol, which was successively tosylated and reduced to give 1,3-diethyladamantane (II). Bromination of II gave 83.8% 3,5-diethyl-1-bromoadamantane, which was successively treated with AcNH2 and KOH to give I (R1-2 = Et, R3 = H). The compds. were evaluated (DA) using a battery of three murine bioassays, including stimulation of locomotor activity, induction of circling in animals with unilateral striatal lesions, and reversal of reserpine α-methyltyrosine induced akinesia. Apparent mechanistic differences were seen between the Me-substituted series and the Et-substituted series. While activities in both series increase with increasing lipophilicity, the Me series as well as amantadine itself, exhibits only indirect DA agonist activity, as evidenced by ipsilateral rotation in the circling model and no significant difference from control in reversal of akinesia. The Et series exhibits weak but reproducible direct DA agonist activity, as shown by contralateral rotation in the circling assay for I (R1 = Et, R2-3 = H) and reversal of akinesia by I (R1 = Et; R2-3 = H; R1-2 = Et, R3 = H). I (R1 = Pr, R2-3 = H) was devoid of any DA agonist activity.

ACCESSION NUMBER: 1982:19721 CAPLUS
DOCUMENT NUMBER: 96:19721
TITLE: Structure-anti-Parkinson activity relationships in the aminoadamantanes. Influence of bridgehead substitution
AUTHOR(S): Henkel, James G.; Hane, Jeffrey T.; Gianutsos, Gerald
CORPORATE SOURCE: Sch. Pharm., Univ. Connecticut, Storrs, CT, 06268, USA
SOURCE: Journal of Medicinal Chemistry (1982), 25(1), 51-6
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 96:19721

IT **41100-52-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 38 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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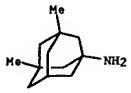
L2 ANSWER 39 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB Human blood platelets were incubated with drugs which either liberated only 5-HT [50-67-9] (incomplete release reaction) or 5-HT as well as ATP [56-65-5]/ADP [58-64-0] (complete release reaction) from subcellular storage organelles. The incomplete release reaction induced by tyramine [51-67-2], tryptamine [61-54-1], and 1-aminoadamantane-HCl [665-66-7] was followed by an increased 5-HT uptake which was enhanced up to 350% as compared with the untreated platelets. After treatment with drugs like 1-amino-3,5-dimethyladamantane-HCl [41100-52-1], imipramine [50-49-7], and reserpine [50-55-5], which induced the complete release reaction, platelets took up significantly less 5-HT as compared with the controls. Apparently, the metabolically inert ATP within the storage organelles is necessary for 5-HT uptake and storage. The uptake of radioactively labeled adenine [73-24-5] and the synthesis of metabolically active adenine nucleotides were increased after preincubation with both types of release-inducing substances. The newly synthesized ATP may serve to restore the metabolically active, cytoplasmic ATP which is consumed either for the extrusion process during the complete release reaction or for the energy-requiring 5-HT reuptake observed after treatment with 5-HT displacing agents.

ACCESSION NUMBER: 1981:417964 CAPLUS
DOCUMENT NUMBER: 95:17964
TITLE: 5-Hydroxytryptamine and adenine uptake by human blood platelets following the release reaction
AUTHOR(S): Wesemann, W.; Von Pusch, I.
CORPORATE SOURCE: Inst. Physiol. Chem., Philipps-Univ. Marburg, Marburg, Fed. Rep. Ger.
SOURCE: Thrombosis Research (1981), 21(4-5), 367-74
CODEN: THBRAA; ISSN: 0049-3848
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 41100-52-1
RL: BIOL (Biological study)
(blood platelet uptake of adenine and hydroxytryptamine response to)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



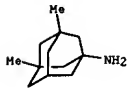
● HCl

L2 ANSWER 40 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
GI

AB Rat brain synaptosomes incorporated serotonin creatinine sulfate (I) [971-74-4] with 2 different uptake mechanisms, high affinity: Kt1 = 47 nM and low affinity: Kt2 = 660 nM. Both uptake mechanisms were noncompetitively inhibited by the potential antiparkinson drugs 1-aminoadamantane-HCl (II-HCl) [665-66-7] (Ki1 = 57 μM, Ki2 = 96 μM) and 1-amino-3,5-dimethyladamantane-HCl (III) [41100-52-1] (Ki1 = 97 μM, Ki2 = 150 μM). The incorporated I was released from synaptosomes on incubation with high concns. (0.5-5 mM) of the drugs or on elec. stimulation with rectangular pulse of alternating polarity. Subthreshold concns. of these drugs (5-50 μM) which are too low to liberate I increased the elec. stimulated release of I. The effect of II, III, and elec. stimulation on dopamine [51-61-6] release paralleled the results observed with I. The uptake of I into isolated synaptic vesicles and the binding to isolated nerve ending membranes was noncompetitively inhibited by 1-aminoadamantanes. III inhibited the binding of I to membranes more effectively (Ki = 0.95 mM) than its uptake into vesicles (Ki = 1.2 mM) contrasting with II which was a weaker inhibitor affecting vesicular uptake (Ki = 2.5 mM) slightly more than membrane binding (Ki = 3.1 mM). In addition to other mechanisms like receptor stimulation, 1-aminoadamantanes may act in parkinsonian patients by enriching the transmitter content in the synaptic cleft.

ACCESSION NUMBER: 1979:432708 CAPLUS
DOCUMENT NUMBER: 91:32708
TITLE: In vitro studies on the possible effects of 1-aminoadamantanes on the serotonergic system in parkinsonism
AUTHOR(S): Wesemann, W.; Dette-Wildenhahn, G.; Fellehner, H.
CORPORATE SOURCE: Physiol.-Chem. Inst. II, Philipps-Univ., Marburg/Lahn, Fed. Rep. Ger.
SOURCE: Journal of Neural Transmission (1972-1989) (1979), 44(4), 263-85
CODEN: JNTMAH; ISSN: 0300-9564
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 41100-52-1
RL: BIOL (Biological study)
(serotonin metabolism by brain synaptosomes response to)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 40 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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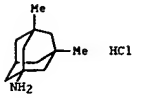
L2 ANSWER 41 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
GI

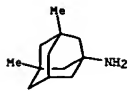


I

AB The effects of memantine (1,3-dimethyl-5-aminoadamantane hydrochloride) (I) [41100-52-1] (10 mg/kg, i.v.) on the stretch-induced reflex tension of flexor muscles extensor digitorum longus and tibialis anterior (EDL/TA) and on the excitability of the neurons relaying transmission in the γ-loop were investigated in decrebrate and spinal cats. I essentially reduced the reflex excitability of flexors EDL/TA induced by fusimotor activity in the decerbrate preparation The drug did not stimulate the reflex activity in acute spinal cats. I suppressed largely the transmission of the fusimotor reflex in the decerebrate as well as in the spinal preparation, although in spinal cats I increased the average firing rate of muscle spindle primaries originating from EDL/TA muscles. The possible mechanism of action of the compound on dopaminergic and serotonergic systems as well as its basic effects on neuronal membranes is discussed.

ACCESSION NUMBER: 1977:545745 CAPLUS
DOCUMENT NUMBER: 87:145745
TITLE: Effects of 1,3-dimethyl-5-aminoadamantane hydrochloride (DMAA) on the stretch-induced reflex tension of flexor muscles and the excitability of the γ-loop in decerebrate and spinal cats
AUTHOR(S): Wand, P.; Sontag, K. H.; Cremer, H.
CORPORATE SOURCE: Dep. Biochem. Pharmacol., Max-Planck-Inst. Exp. Med., Goettingen, Fed. Rep. Ger.
SOURCE: Arzneimittel-Forschung (1977), 27(7), 1477-81
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 41100-52-1
RL: BIOL (Biological study)
(muscle stretch reflex response to, in decerebrate and spinal animals, γ-motor neurons in relation to)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L2 ANSWER 41 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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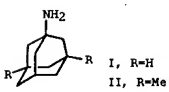
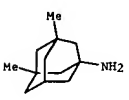
L2 ANSWER 42 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
GI



I, R=H
II, R=Me

AB Amantadine-HCl (I-HCl) [665-66-7] and D-145-HCl (II-HCl) [41100-52-1] administered either i.p. or orally to rats at 50-100 mg/kg were rapidly absorbed. Between 20 and 25% I and 6-11% II were excreted unchanged in the urine, this excretion being maximum 2 h after administration. 1-Amino-3-hydroxyadamantane [702-82-9] was the only I metabolite detected, whereas 1-hydroxy-3,5-dimethyladamantane [707-37-9], 1-amino-3-hydroxymethyl-5-methyladamantane [58850-55-8], 1-amino-4-hydroxy-3,5-dimethyladamantane [58850-54-7], and 1-amino-7-hydroxy-3,5-dimethyladamantane [63971-25-5] were II metabolites. Following oral administration of 10 mg II to a human volunteer, I and 1-amino-3-hydroxymethyl-5-methyladamantane were excreted in the urine.

ACCESSION NUMBER: 1977:526940 CAPLUS
DOCUMENT NUMBER: 87:126940
TITLE: Gas chromatographic and mass spectrometric studies on metabolites of amino adamantane excreted in urine
AUTHOR(S): Wesemann, W.; Schollmeyer, J. D.; Sturm, G.
CORPORATE SOURCE: Inst. Physiol. Chem. II, Philipps-Univ., Marburg, Fed. Rep. Ger.
SOURCE: Arzneimittel-Forschung (1977), 27(7), 1471-7
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
IT 41100-52-1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



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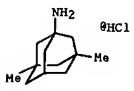
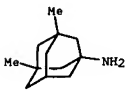
L2 ANSWER 43 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
GI



I

AB Nerve endings isolated from rat brain accumulated exogenous serotonin [50-67-9] and dopamine [51-61-6]. Both biogenic amines were released by elec. stimulation and by incubation with 5 + 10-5 - 5 + 10-4 M 1-aminoadamantane-HCl [665-66-7] and 1-amino-3,5-dimethyladamantane-HCl (I) [41100-52-1]; the elec.-stimulated release was small and could be significantly increased after simultaneous incubation of nerve endings with subthreshold concns. (5 + 10-6 - 5 + 10-5 M) of the adamantane derivs. The reuptake of released serotonin was noncompetitively inhibited by the adamantanes. Serotonin uptake by blood platelets was also inhibited by small concns. of I (10-5 - 2 + 10-4 M). High I concns. (>2 + 10-3 M) induced simultaneous release of serotonin, ATP [56-65-5], and ADP [58-64-0]. At 2 + 10-4 - 2 + 10-3 M I, only serotonin was released.

ACCESSION NUMBER: 1977:511437 CAPLUS
DOCUMENT NUMBER: 87:111437
TITLE: Effect of 1-aminoadamantanes. Comparative investigations with isolated nerve endings and blood platelets on the release of serotonin and dopamine
AUTHOR(S): Haacke, U.; Sturm, G.; Suewer, V.; Wesemann, W.; Wildenhahn, G.
CORPORATE SOURCE: Physiol.-Chem. Inst. II, Philipps-Univ., Marburg, Fed. Rep. Ger.
SOURCE: Arzneimittel-Forschung (1977), 27(7), 1481-3
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
IT 41100-52-1
RL: BIOL (Biological study)
(dopamine and serotonin release by blood platelet and brain nerve endings response to)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

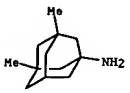
L2 ANSWER 43 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L2 ANSWER 44 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
GI For diagram(s), see printed CA Issue.
AB Eight adamantanes (I, R = NH2, NHMe, NMe2, NMeCHMe2, or cyclohexylamino; R1, R2. = C1-4 alkyl) and their salts, used in the treatment of parkinsonism, were prepared from I (R = Cl or Br) and urea and derivs. The activity of I.HCl (R = NH2, R1 = R2 = Me) (II.HCl) in the central nervous system was tested i.p. in the mouse and rat. Thus, I (R = Cl, R1 = R2 = Me) and urea were heated at 220° to give, after treatment with HCl, 78% II.HCl. Methylation of II with HCHO and HCO2H gave, after HCl-treatment, 77% I (R = NMe2, R1 = R2 = Me).
ACCESSION NUMBER: 1975:86248 CAPLUS
DOCUMENT NUMBER: 82:86248
TITLE: 3,5-Dialkyl-1-aminoadamantanes for the treatment of parkinsonism
INVENTOR(S): Scherm, Arthur; Peteri, Dezso
PATENT ASSIGNEE(S): Merz und Co.
SOURCE: Ger. Offen., 20 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2318461	A1	19741031	DE 1973-2318461	19730412
BE 798450	A1	19730816	BE 1973-130199	19730419
NL 7305644	A	19731023	NL 1973-5644	19730419
AT 7303530	A	19750815	AT 1973-3530	19730419
AT 329532	B	19760510		
CA 974518	A1	19750916	CA 1973-169484	19730419
ES 413944	A1	19760601	ES 1973-413944	19730419
PL 89158	P	19761030	PL 1973-162028	19730419
CH 603545	A	19780831	CH 1973-5686	19730419
FR 2182998	A1	19731214	FR 1973-14690	19730420
JP 49018860	A2	19740219	JP 1973-44965	19730420
US 4122193	A	19781024	US 1973-352893	19730420
GB 1393503	A	19750507	GB 1973-19436	19730424

PRIORITY APPLN. INFO.: DE 1972-2219256 A 19720420
DE 1973-2318461 A 19730412

IT 41100-52-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and use in the treatment of parkinsonism)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



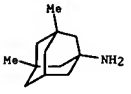
● HCl

L2 ANSWER 44 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L2 ANSWER 45 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN
GI For diagram(s), see printed CA Issue.
AB Aminoadamantanes (I, R = Me, Et; R1, R2, R3 = H, Me) were prepared by treating halo adamantanes (II) with R3NHCONHR3 at 165-85°.
ACCESSION NUMBER: 1973:124152 CAPLUS
DOCUMENT NUMBER: 78:124152
TITLE: Aminoadamantanes and their salts
INVENTOR(S): Burkhard, Jiri; Landa, Stanislav
SOURCE: Czech., 3 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 146405		19721215	CS 1970-5509	19700806

IT 41100-52-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

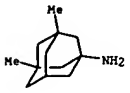
L2 ANSWER 46 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

AB To assess the possible pharmacodynamic effects of the sym. lipophilic adamantyl group, a number of N-arylsulfonyl-N'-adamantylureas, ArSO2NHCONHR (I), were prepared for evaluation as hypoglycemic agents. (All m.ps. were taken in sealed, submerged capillary tubes). Adamantane-1-carboxamide (9 g.) in 200 ml. dry Et2O added to 10 g. LiAlH4 suspended in 500 ml. dry Et2O with stirring, the mixture refluxed 4 hrs., cooled to -5° with stirring, treated dropwise by 10 ml. H2O, followed by 30 ml. 10% aqueous NaOH and 10 ml. H2O, the solids filtered off and washed with 500 ml. Et2O, the combined Et2O solns. dried and evaporated in vacuo, the residue dissolved in 50 ml. Et2O, and the solution filtered and treated with dry HCl gave 7 g. 1-aminomethyladamantane-HCl, m. 320° (EtOH). 1-Methyladamantane brominated by the procedure reported for 1-bromoadamantane (Stetter, et al., CA 53, 21709f; 54, 1356a) gave 93% 3-methyl-1-bromoadamantane (II), b0.05 65-7°, whose structure was supported by its nuclear magnetic resonance (n.m.r.) spectrum. From II was prepared by the MeCN-H2SO4 method (S., et al., CA 54, 9950d) 1-acetamido-3-methyladamantane (III), m. 108-9° (sublimation at 90-100°/0.05 mm.). Deacetylation of III by KOH in O(CH2CH2OH)2, followed by Et2O extraction gave an Et2O solution containing product and .apprx.5% unchanged III, which was treated with dry HCl to give 87% 1-amino-3-methyladamantane-HCl, m. 295-300°. 1,3-Dimethyladamantane brominated as above gave 77.5 g. 1-bromo-3,5-dimethyladamantane (IV), b0.03 67-9°, n25D 1.5178 (structure supported by n.m.r. spectrum), which was converted into 96% 1-acetamido analog of IV, m. 80-2° (sublimation), and the latter into 87% 1-amino analog of IV HCl salt, m. 290-5°. Adamantane (V) (100 g.) and 85 g. tert-BuCl in 400 ml. anhydrous cyclohexane treated portionwise during 8 hrs. with 4.6 g. (total) AlCl3 (in 0.5 g. batches AlCl3), when the reaction was complete (as judged from escaping isobutane gas), 100 ml. N HCl added with stirring, followed by 500 ml. Et2O, and the organic layer separated, washed with 50 ml. cold H2O and 50 ml. 5% aqueous NaHCO3, dried, and evaporated in vacuo gave 115 g. crude 1-chloroadamantane (VI), m. 152-6°, containing (gas chromatography) 90-5% VI and 5-10% V; recrystn. of a sample from EtOH at - 50° gave pure VI, as determined by mixed m.p. with authentic VI and by x-ray diffraction patterns. Crude VI was converted by the MeCN-H2SO4 method into 83% crude 1-acetamidoadamantane (VII), m. 144-6°; pure VII m. 147-9° (EtOH). Crude VII (108 g.) saponified gave 51 g. pure 1-aminoadamantane (VIII), m. 160-200°. VIII (302.5 g.) and 535 g. 4-MeC6H4SO2NHCO2Et in 6 l. dry PhMe refluxed 5 hrs., cooled to room temperature, the crystalline solid filtered off and dissolved (without application of heat) in .apprx.2 l. CHCl3 which had previously been shaken with 50 g. Al2O3 to remove traces EtOH, the solution washed with cold 5% HCl and H2O until neutral, dried (MgSO4), concentrated in vacuo to 1/2 its volume, warmed to 50°, diluted with hot petr. ether (b. 60-71°) to start crystallization, and chilled overnight gave 400 g. I (Ar = 4-MeC6H4, R = 1-adamantyl) (IX), m. 178-9° (CHCl3-petr. ether). The following I were prepared (Ar, R, m.p., relative potency with respect to hypoglycemic activity given): 4-MeC6H4, Bu (Tolbutamide), -, 1; 4-MeC6H4, 1-adamantyl, 178-9°, 15.5; 4-MeC6H4, cyclohexyl (Tolcyclamide), -, 12.8; 4-EtC6H4, 1-adamantyl, 153-5°, 14.8; 4-EtC6H4, cyclohexyl, -, 9.3; 4-MeSC6H4, 1-adamantyl, 155-8°, 8.7; 4-MeSC6H4, cyclohexyl (Thiohexamide), -, 4.1; 4-ClC6H4, 1-adamantyl, 150-1°, 5.1; 4-ClC6H4, cyclohexyl, -, 5.6; 4-ClC6H4, Pr, -, 2.1; 4-iso-PrC6H4, 1-adamantyl, 190-2°, 2.9; 4-AcC6H4, 1-adamantyl, 163-5°,

L2 ANSWER 46 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

1.6; 4-AcC6H4, cyclohexyl (Acetohexamide), -, 4.0; 4,3-Me(H2N)C6H3, 1-adamantyl, 175° (decompn.), 0; 4,3-Me(H2N)C6H3, cyclohexyl (Metahexamide), -, 5.0; 4-MeC6H4, 2-adamantyl, 206-8°, 4.0; 4-MeC6H4, 3-methyl-1-adamantyl, 184-6°, 2.8; 4-MeC6H4, 3,5-dimethyl-1-adamantyl, 166-8°, 0; 4-EtC6H4, 1-adamantylmethyl, 203-5°, 0.2; 4-AcC6H4, 1-adamantylmethyl, 204-6°, 0. The pharmacol. evaluation of the compds. is discussed; particularly with respect to IX. Preliminary clinical data thus far indicate IX to be a most satisfactory, potent oral hypoglycemic agent with an effective av. dose, single or divided, of 400 mg./day. IX is equal to Chlorpropamide on a wt. basis and possesses about 5 times the potency of Tolbutamide. The activity of IX is rapid in onset with tentative duration of 4-6 hrs., indicating that IX is rapidly absorbed and utilized by the body.

ACCESSION NUMBER: 1964:23043 CAPLUS
DOCUMENT NUMBER: 60:23043
ORIGINAL REFERENCE NO.: 60:4022f-h,4023a-e
TITLE: Adamantyl group in medical agents. I. Hypoglycemic N-arylsulfonyl-N'-adamantylureas
AUTHOR(S): Gerzon, Koert; Krumalns, Eriks V.; Brindle, Richard L.; Marshall, Frederick J.; Root, Mary A.
CORPORATE SOURCE: Lilly Res. Labs., Indianapolis, IN
SOURCE: Journal of Medicinal Chemistry (1963), 6(6), 760-3
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT 41100-52-1, 1-Adamantanamine, 3,5-dimethyl-, hydrochloride (preparation of)
RN 41100-52-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, 3,5-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

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FILE LAST UPDATED: 10 Jun 2005  (20050610/ED)

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